REMARKS

The present Amendment is in response to the Examiner's Final Office Action mailed October 10, 2001. Under 37 C.F.R. §1.116, Applicants cancel claim 39 and amend claims 41 and 44 to comply with the Examiner's requirement set forth in the Office Action. Claims 1-9, 14, 18-24, and 36-38, and 40-45 are pending.

Applicants express appreciation to the Examiner for conducting a telephone interview with Applicants on December 7, 2001. Reconsideration of the application is respectfully requested in view of the above amendments to the claims and the following remarks. For the Examiner's convenience and reference, Applicants' remarks are presented in the order in which the corresponding issues were raised in the Office Action.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "**Version with markings to show changes made**."

1. Rejections under 35 U.S.C. § 112, First Paragraph

The Examiner rejects claims 1, 2, 22, and 36-45 under 35 U.S.C. § 112, First Paragraph for insufficient written description.

As evidence of written support for claim 1 as amended, Applicants respectfully direct the Examiner's attention to the Specification at page 28, line 28, where the diversity of an embodiment of the tester protein, antibody, is specified to be at least 10^7.

As evidence of written support for claim 2 as amended, Applicants respectfully direct the Examiner's attention to the Specification at page 36, line 25, where support for the term "the reconstituted transcription activator" appears.

As evidence of written support for claim 22 as amended, Applicants respectfully direct the Examiner's attention to the Specification at page 45, line 13, where support for the term "growth factor receptor" appears.

As evidence of written support for claims 36-38 as amended, Applicants respectfully direct the Examiner's attention to the Specification at page 23, lines 2-12, where support for the terms "human, non-human primates, or rodents" and "immunoglobulin gene" appears.

As evidence of written support for claims 36-38, Applicants respectfully direct the Examiner's attention to the Specification at page 23, lines 2-12, where support for the terms "human, non-human primates, or rodents" and "immunoglobulin gene" appears.

As evidence of written support for claims 41-43, Applicants respectfully direct the Examiner's attention to claim 18 as originally filed. Claim 41 is essentially claim 18 rewritten in an independent form with addition of steps (g)-(j) according to the Examiner's suggestion. Support for steps (g)-(j) appears at the Specification, page 92, lines 17-24.

As evidence of written support for claims 44 and 45, Applicants respectfully direct the Examiner's attention to the Specification at page 45, line 13, where support for the term "growth factor receptor" appears.

2. Rejections under 35 U.S.C. § 112, Second Paragraph

The Examiner rejects claims 41 and 44 under 35 U.S.C. § 112, Second Paragraph for being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants amend claims 41 and 44 to address the issue of lacking antecedent basis for the limitation in the claims as to the terms "the transcription factor", "the first" or "second polypeptide subunit", and "the reporter gene".

The Examiner also rejects claim 41 under 35 U.S.C. § 112, Second Paragraph for being incomplete for omitting essential steps. Applicants disagree with the Examiner's position that essential steps are missing and reserve the right to reintroduce the claims in a subsequent application. In the meantime and purely for the purpose of expediting the prosecution of the application, Applicants amend claim 41 to add steps (h)-(j).

Applicants submit that claims 41 and 44 as amended are sufficiently definite and well understood by one of ordinary skill in the art. Withdrawal of the rejection under 35 U.S.C. § 112, Second Paragraph is therefore respectfully requested.

3. Rejections under 35 U.S.C. § 103(a)

1) Rejection in view of Nandabalan et al., Hoeffler et al. and Hua et al.

The Examiner rejects claims 1-9, 14, 20-24, and 36-40 under 35 U.S.C. §103(a) for being unpatentable over Nandabalan et al. (US Patent No: 6,057,101), Hoeffler et al. (1999, WO 99/28502) and Hua et al. (1997) Plasmid 38:91-96.

As the Examiner acknowledges, Nandabalan et al., fails to teach the claimed method of screening a library of tester proteins containing two independently varying subunits and with a diversity of $1x10^7$ or higher as specified by independent claim 1.

Hoeffler et al. and Hua et al., alone or in combination, do not teach or suggest the

elements missing in Nandabalan et al. During the interview, the Examiner agreed that Hoeffler et al. and Hua et al. fail to teach or suggest to one of ordinary skill in the pertinent art to increase the diversity of the tester protein library to be $1x10^7$ or higher, especially in view of the statement by Hoeffler et al. that "[t]he diversity of the library doesn't need to be much above 10^6 since the transformation capacity of yeast is generally 10^7 or below". Page 55, lines 2-3. Hua et al. meanwhile does not teach screening a library of proteins, let alone suggesting increasing the diversity of a library as specified by independent claim 1 to be $1x10^7$ or higher. Hua et al's general statement of desirability of simplifying the cloning process for functional analysis of a **new gene** also does not suggest constructing a library of tester proteins as specified in the claims with a diversity $1x10^7$ or higher. Thus, the cited references, alone or in combination, fail to teach or suggest the claimed invention under 35 U.S.C. § 103(a). Withdrawal of this ground of rejection is therefore respectfully requested.

2) Rejection in view of Nandabalan et al., Hoeffler et al. and Gietz et al.

The Examiner rejects claims 1-9, 14, 20-24, and 36-40 under 35 U.S.C. §103(a) for being unpatentable over Nandabalan, Hoeffler et al. and Gietz et al. (1995) Methods in Molecular and Cell Biology 7(3):254-269.

As discussed above, both Nandabalan et al. and Hoeffler et al. fail to teach or suggest the claimed method of screening a library of tester proteins containing two independently varying subunits and with a diversity of $1x10^7$ or higher as specified by independent claim 1.

During the interview, the Examiner agreed that the third reference, Gietz et al., fails to teach or suggest screening a library of proteins with a diversity of $1x10^7$ or higher. Instead, Gietz et al teaches that "[f]or libraries of **$1x10^6$ independent clones** [i.e., diversity or complexity of the clones] or more, large numbers of transformants are needed to ensure that the entire library has been screened". Page 266, left column, under "DISCUSSION", lines 10-12. To cover such libraries with diversity of $1x10^5$, Gietz et al had to screen as many as **$5.2x10^7$ transformants** from a single scaled-up transformation reaction. Page 266, right column, under "DISCUSSION", lines 10-12. Thus, Gietz et al fails to teach screening a library of proteins with **at least $1x10^7$ diversity** as specified by independent claim 1. Thus, the cited references, alone or in combination, fail to teach or suggest the claimed invention under 35 U.S.C. § 103(a). Withdrawal of this ground of rejection is therefore respectfully requested.

3) Rejection in view of Hoeffler et al. and Goodman et al.

The Examiner rejects claims 44-45 under 35 U.S.C. §103(a) for being unpatentable over Hoeffler et al. and Goodman et al. (1996) in "The Pharmacological Basis of Therapeutics" 9th ed.

McGraw Hill Publishing pp1365-1386.

As discussed above and agreed by the Examiner, Hoeffler et al. fail to teach or suggest the claimed method of screening a library of tester proteins containing two independently varying subunits and with a diversity of $1x10^7$ or higher as specified by independent claim 44 as amended.

The secondary reference, Goodman et al., fails to supply the elements not taught by Hoeffler et al. As the Examiner states, Goodman et al. merely describes diseases related to growth hormone deficiency and effects of growth hormones are mediated by the growth hormone receptor.

Thus, the cited references, alone or in combination, fail to teach or suggest the claimed invention under 35 U.S.C. § 103(a). Withdrawal of this ground of rejection is therefore respectfully requested.

4) Rejection in view of Hoeffler et al. and Terret

The Examiner rejects claims 18, 19, and 41-43 under 35 U.S.C. §103(a) for being unpatentable over Hoeffler et al. and Terret (1998) in "Combinatory Chemistry" Oxford University Press pp2-4.

As discussed above and agreed by the Examiner, Hoeffler et al. fail to teach or suggest the claimed method of screening a library of tester proteins containing two independently varying subunits and with a diversity of $1x10^7$ or higher as specified by independent claims 1 and 41 as amended .

The secondary reference, Terret, fails to supply the elements not taught by Hoeffler et al. As the Examiner states, Terret merely teaches the general method of drug discovery including lead discovery and optimization of lead molecules.

Thus, the cited references, alone or in combination, fail to teach or suggest the claimed invention under 35 U.S.C. § 103(a). Withdrawal of this ground of rejection is therefore respectfully requested.

CONCLUSION

In light of the remarks and arguments set forth above, Applicants earnestly believe that they are entitled to a letters patent, and respectfully solicit the Examiner to expedite prosecution of this patent application to issuance. Should the Examiner have any questions, the Examiner is encouraged to telephone the undersigned.

Respectfully submitted,

Date: December 21, 2001

By: _____
Shirley Chen, Ph.D.
Registration No. 44,608

WILSON SONSINI GOODRICH & ROSATI
650 Page Mill Road
Palo Alto, CA 94304-1505
Direct line: (650) 565-3856
Client No. 021971